Safety Data Sheet

Cryptopleurine

Division of Safety
National Institutes
of Health

WARNING!

THIS COMPOUND IS HIGHLY TOXIC AND A POWERFUL SKIN IRRITANT AND VESICANT. IT IS READILY ABSORBED THROUGH THE INTESTINAL TRACT. AVOID FORMATION AND BREATHING OF AEROSOLS.

LABORATORY OPERATIONS SHOULD BE CONDUCTED IN A FUME HOOD, GLOVE BOX, OR VENTILATED CABINET.

AVOID SKIN CONTACT: IF EXPOSED, WASH WITH SOAP AND COLD WATER. AVOID WASHING WITH SOLVENTS AND EXPOSURE TO UV LIGHT. AVOID RUBBING OF SKIN OR INCREASING ITS TEMPERATURE.

FOR EYE EXPOSURE, IRRIGATE IMMEDIATELY WITH LARGE AMOUNTS OF WATER. FOR INGESTION, DRINK MILK OR WATER. REFER FOR GASTRIC LAVAGE. FOR INHALATION, REMOVE VICTIM PROMPTLY TO CLEAN AIR. ADMINISTER RESCUE BREATHING IF NECESSARY. REFER TO PHYSICIAN.

IN CASE OF LABORATORY SPILL, WEAR PROTECTIVE CLOTHING DURING CLEANUP. AVOID SKIN CONTACT OR BREATHING OF AEROSOLS. USE 5 mM HCl TO DISSOLVE COMPOUND. DISPOSE OF WASTE SOLUTIONS AND MATERIALS APPROPRIATELY.

A. Background

Cryptopleurine (CP) is a highly toxic skin irritant and vesicant extracted from the bark of Cryptocaria pleurosperma, specifically active against Eagle's 9KB carcinoma of the nasopharynx in cell culture. It is a white crystalline solid, practically insoluble in water and most organic solvents. Its toxic action seems to be due to binding to eukaryotic ribosomes and inhibition of translocation in protein synthesis.

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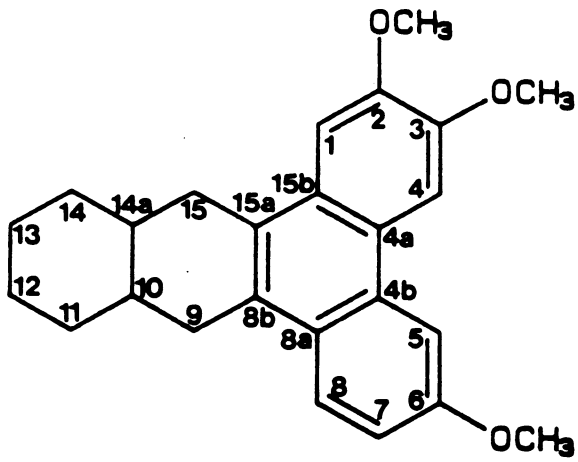
B. Chemical and Physical Data

1. Chemical Abstract Nos.: 482-22-4; 87302-53-2 for the optical (S-) isomer; 23365-52-8 for the racemic form.

2. Synonyms: Cryptopleurine;[A] 9-H-phenanthro[9,10-b]quinolizine, 11,12,13,14,14a,15-hexahydro-2,3,6-trimethoxy-(R)-.[B]

3. Chemical structure and molecular weight:



$C_{24}H_{27}NO_3$; 377

4. Density: No data.

5. Optical rotation: $[\alpha]_D^{18} = -105°$ (in $CHCl_3$) (Gellert et al., 1978).

6. Absorption spectroscopy: UV absorption maxima (log ε) are: 258(4.62), 286(4.40), 343(2.96), 359(2.68). IR spectral data have been published (Gellert and Riggs, 1954).

7. Volatility: No data; may be assumed to be low.

8. Solubility: Practically insoluble in water, methanol, ethanol and acetone; soluble in chloroform and ether (De la Lande, 1948). For biological experiments cryptopleurine is dissolved in 5 mM HCl (Dölz et al., 1980).

9. Description: Colorless needles. pK_a in 70% aqueous methanol= 7.55 (Gellert and Riggs, 1954).

10. Boiling point: No data; melting point: 197-198°C.

[A] Chemical Abstracts name, used for listings in 8th Decennial Index.
[B] Chemical Abstracts name, used for listings in 9th Decennial Index and subsequently.

11. Stability: Solutions of CP in 5 mM HCl are stable for at least 6 months if kept at -25°C; solutions in chloroform or aqueous solutions of the sulfate are "unstable" (conditions not described). Solid CP is sensitive to light, turning yellow on prolonged exposure in air (Gellert and Riggs, 1954).

12. Chemical reactivity: No data; it may be assumed that CP is attacked by strong oxidizing agents.

13. Flashpoint: No data.

14. Autoignition temperature: No data.

15. Explosive limits in air: No data.

Fire, Explosion, and Reactivity Hazard Data

1. CP does not require special fire-fighting procedures or equipment and does not present unusual fire and explosion hazards.

2. The presence of strong oxidants probably contributes to the instability of CP.

3. No other incompatibilities are known.

4. CP does not require non-spark equipment.

Operational Procedures

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens describe operational practices to be followed when potentially carcinogenic chemicals are used in NIH laboratories. The NIH Guidelines should be consulted to identify the proper use conditions required and specific controls to be implemented during normal and complex operations or manipulations involving CP.

It should be emphasized that this data sheet and the NIH Guidelines are intended as starting points for the implementation of good laboratory practices when using this compound. The practices and procedures described in the following sections pertain to the National Institutes of Health and may not be universally applicable to other institutions. Administrators and/or researchers at other institutions should modify the following items as needed to reflect their individual management system and current occupational and environment regulations.

1. Chemical inactivation: No validated method reported.

2. Decontamination: Turn off equipment that could be affected by CP or the materials used for cleanup. If there is any uncertainty regarding the procedures to be followed for

decontamination, call the NIH Fire Department (dial 116) for assistance. Wipe off surfaces with 5 mM HCl, then wash with copious quantities of water. Glassware should be rinsed (in a hood) with 5 mM HCl, followed by soap and water. Animal cages should be washed with water.

3. Disposal: No waste streams containing CP shall be disposed of in sinks or general refuse. Surplus CP or chemical waste streams contaminated with CP shall be handled as hazardous chemical waste and disposed of in accordance with the NIH chemical waste disposal system. Nonchemical waste (e.g., animal carcasses and bedding) containing CP shall be handled and packaged for incineration in accordance with the NIH medical-pathological waste disposal system. Potentially infectious waste (e.g., tissue cultures) containing CP shall be disinfected by heat using a standard autoclave treatment and packaged for incineration, as above. Burnable waste (e.g., absorbent bench top liners) minimally contaminated with CP shall be handled as potentially infectious waste and packaged for incineration, as above. Absorbent materials (e.g., associated with spill cleanup) grossly contaminated shall be handled in accordance with the chemical waste disposal system. Radioactive waste containing CP shall be handled in accordance with the NIH radioactive waste disposal system.

4. Storage: Store solid CP and its solutions in dark-colored, tightly closed containers, preferably under refrigeration. Avoid exposure to light and moisture. Store working quantities of CP and its solutions in an explosion-safe refrigerator in the work area.

Monitoring and Measurement Procedures Including Direct Field Measurements and Sampling for Subsequent Laboratory Analysis

There are no published procedures for the analysis of CP.

Biological Effects (Animal and Human)

1. Absorption: No data. CP is a vesicant but there is no information whether systemic toxic effects are produced by absorption through the skin. CP appears to be readily absorbed from the gastrointestinal tract since it is as toxic orally as it is parenterally.

2. Distribution and pharmacokinetics: No data.

3. Metabolism and excretion: No data.

4. Toxic effects: CP is highly toxic in all mammalian species tested. The LD50 (in mg/kg) is 2.5-5 (mouse, subcutaneous), 1.5 (rabbit, intravenous), and 2-3 (rabbit, oral). Doses of 1 and 1.5 mg/kg killed a cat and a dog, respectively. The toxic action in these species is slow, with usually no symptoms until 12 hours after administration, and death in 24-48 hours even

after high doses. In rabbits, lethal doses produce diarrhea and inflammation of the gastric mucosa after oral (but not after intravenous) administration. No marked changes have been noted in liver, kidney, lung, or trachea following parenteral dosage.

CP is a powerful skin irritant. In man, there is a delay of 1-3 days following topical application, progressing from erythema to thickening of the skin, formation of fluid pockets, and desquamation (De la Lande, 1948). Its mechanism of action seems to be binding to eukaryotic ribosomes with consequent inhibition of translocation (Dölz et al., 1980).

5. Carcinogenic effects: None reported. CP is a cytotoxic agent with specific high activity against Eagle's 9KB carcinoma of the nasopharynx in cell culture. It is inactive against a variety of other neoplasms (Farnsworth et al., 1969).

6. Mutagenic and teratogenic effects: None reported.

G. Emergency Treatment

1. Skin and eye exposure: For skin exposure, remove contaminated clothing and wash skin with soap and water. Skin should not be rinsed with organic solvents or scanned with UV light. Since CP is a strong skin irritant and vesicant, avoid rubbing of skin or increasing its temperature. For eye exposure, irrigate immediately with copious quantities of running water for at least 15 minutes. Obtain ophthalmological evaluation.

2. Ingestion: Drink plenty of water or milk. Vomiting might reexpose the mouth and esophagus. Refer for gastric lavage.

3. Inhalation: Remove victim promptly to clean air. Administer rescue breathing if necessary.

4. Refer to physician at once. Consider treatment for pulmonary irritation.

H. References

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J Chem 31:2095-2097.